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Index
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NEWS 6 Oct 22 Over 1 million reactions added to CASREACT
NEWS 7 Oct 22 DGENE GETSIM has been improved
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NEWS 9 Nov 19 New Search Capabilities USPATFULL and USPAT2
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NEWS 13 Nov 30 Files VETU and VETB to have open access
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NEWS 18 Dec 17 New fields for DPCI
NEWS 19 Dec 19 CAS Roles modified
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NEWS 24 Feb 01 DKILIT now produced by FIZ Karlsruhe and has a new update
frequency
NEWS 25 Feb 19 Access via Tymnet and SprintNet Eliminated Effective 3/31/02
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=> s formoterol
L1 2604 FORMOTEROL

=> s fluticasone propionate
L2 3662 FLUTICASONE PROPIONATE

=> s l1 ad l2
MISSING OPERATOR L1 AD
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l1 and l2
L3 179 L1 AND L2

=> s sodium chloride or saline
L4 600269 SODIUM CHLORIDE OR SALINE

=> s citric acid
L5 140111 CITRIC ACID

=> s l3 and l4 and l5
L6 3 L3 AND L4 AND L5

=> d l6 1-3

L6 ANSWER 1 OF 3 USPATFULL
AN 2001:187017 USPATFULL
TI Closure-cap and container as a two-chamber cartridge for nebulisers for
producing aerosols and active substance formulations, suitable for
storage
IN Hochrainer, Dieter, Bingen, Germany, Federal Republic of
Zierenberg, Bernd, Bingen, Germany, Federal Republic of
PI US 2001032643 A1 20011025
AI US 2001-871500 A1 20010531 (9)

RLI Continuation of Ser. No. US 1999-416476, filed on 12 Oct 1999, PENDING
PRAI DE 1998-19847968 19981017
DE 1998-19847970 19981017
DT Utility
FS APPLICATION
LN.CNT 1291
INCL INCLM: 128/200.210
INCLS: 604/415.000
NCL NCLM: 128/200.210
NCLS: 604/415.000
IC [7]
ICM: A61M005-32
ICS: A61B019-00

L6 ANSWER 2 OF 3 USPATFULL
AN 2001:90260 USPATFULL
TI Fatty acid-pharmaceutical agent conjugates
IN Webb, Nigel L., Bryn Mawr, PA, United States
Bradley, Matthews O., Laytonsville, MD, United States
Swindell, Charles S., Merion, PA, United States
Shashoua, Victor E., Brookline, MA, United States
PI US 2001002404 A1 20010531
AI US 2000-730450 A1 20001205 (9)
RLI Continuation of Ser. No. US 1996-651428, filed on 22 May 1996,
ABANDONED
DT Utility
FS APPLICATION
LN.CNT 2511
INCL INCLM: 514/560.000
INCLS: 514/558.000
NCL NCLM: 514/560.000
NCLS: 514/558.000
IC [7]
ICM: A61K031-20
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 3 OF 3 USPATFULL
AN 1998:98932 USPATFULL
TI DHA-pharmaceutical agent conjugates of taxanes
IN Shashoua, Victor E., Brookline, MA, United States
Swindell, Charles S., Merion, PA, United States
Webb, Nigel L., Bryn Mawr, PA, United States
Bradley, Matthews O., Laytonsville, MD, United States
PA Neuromedica, Inc., Conshohocken, PA, United States (U.S. corporation)
PI US 5795909 19980818
AI US 1996-651312 19960522 (8)
DT Utility
FS Granted
LN.CNT 2451
INCL INCLM: 514/449.000
INCLS: 514/549.000
NCL NCLM: 514/449.000
NCLS: 514/549.000
IC [6]
ICM: A61K031-335
ICS: A61K031-22
EXF 514/449; 514/549
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> s 14 and 13
L7 10 L4 AND L3

=> dup rem 17
PROCESSING COMPLETED FOR L7
L8 10 DUP REM L7 (0 DUPLICATES REMOVED)

=> d 18 1-19

L8 ANSWER 1 OF 10 USPATFULL
AN 2002:30480 USPATFULL
TI Phospholipid-based powders for inhalation
IN Weers, Jeffry G., Half Moon Bay, CA, UNITED STATES
Tarara, Thomas E., Burlingame, CA, UNITED STATES
Clark, Andrew, Half Moon Bay, CA, UNITED STATES
PI US 2002017295 A1 20020214
AI US 2001-888311 A1 20010622 (9)
PRAI US 2000-216621 20000707 (60)
DT Utility
FS APPLICATION
LN.CNT 1103
INCL INCLM: 128/203.120
INCLS: 424/043.000
NCL NCLM: 128/203.120
NCLS: 424/043.000
IC [7]
ICM: A61K009-00
ICS: A61K009-14
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8 ANSWER 2 OF 10 USPATFULL
AN 2001:217988 USPATFULL
TI Stabilized preparations for use in metered dose inhalers
IN Weers, Jeffry G., San Diego, CA, United States
Schutt, Ernest G., San Diego, CA, United States
Dellamary, Luis A., San Marcos, CA, United States
Tarara, Thomas E., San Diego, CA, United States
Kabalnov, Alexey, Corvallis, OR, United States
PI US 2001046474 A1 20011129
AI US 2001-862764 A1 20010521 (9)
RLI Division of Ser. No. US 1998-218212, filed on 22 Dec 1998, PENDING
Continuation of Ser. No. WO 1998-US20615, filed on 29 Sep 1998, UNKNOWN
Continuation-in-part of Ser. No. US 1998-133848, filed on 14 Aug 1998,
ABANDONED Continuation-in-part of Ser. No. US 1998-106932, filed on 29
Jun 1998, ABANDONED
PRAI US 1997-60337 19970929 (60)
DT Utility
FS APPLICATION
LN.CNT 2850
INCL INCLM: 424/045.000
NCL NCLM: 424/045.000
IC [7]
ICM: A61L009-04
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8 ANSWER 3 OF 10 USPATFULL
AN 2001:212586 USPATFULL
TI In vivo delivery methods and compositions
IN Kensey, Kenneth R., Malvern, PA, United States
PI US 2001044584 A1 20011122

AI US 2001-819924 A1 20010328 (9)
RLI Continuation-in-part of Ser. No. US 2000-727950, filed on 1 Dec 2000,
PENDING Continuation-in-part of Ser. No. US 2000-628401, filed on 1 Aug
2000, PENDING Continuation-in-part of Ser. No. US 2000-501856, filed on
10 Feb 2000, PENDING Continuation-in-part of Ser. No. US 1999-439795,
filed on 12 Nov 1999, PENDING Continuation-in-part of Ser. No. US
1997-919906, filed on 28 Aug 1997, GRANTED, Pat. No. US 6019735
DT Utility
FS APPLICATION
LN.CNT 2120
INCL INCLM: 600/504.000
INCLS: 600/573.000; 604/066.000; 604/067.000
NCL NCLM: 600/504.000
NCLS: 600/573.000; 604/066.000; 604/067.000
IC [7]
ICM: A61B005-00

L8 ANSWER 4 OF 10 USPATFULL
AN 2001:187017 USPATFULL
TI Closure-cap and container as a two-chamber cartridge for nebulisers for
producing aerosols and active substance formulations, suitable for
storage
IN Hochrainer, Dieter, Bingen, Germany, Federal Republic of
Zierenberg, Bernd, Bingen, Germany, Federal Republic of
PI US 2001032643 A1 20011025
AI US 2001-871500 A1 20010531 (9)
RLI Continuation of Ser. No. US 1999-416476, filed on 12 Oct 1999, PENDING
PRAI DE 1998-19847968 19981017
DE 1998-19847970 19981017
DT Utility
FS APPLICATION
LN.CNT 1291
INCL INCLM: 128/200.210
INCLS: 604/415.000
NCL NCLM: 128/200.210
NCLS: 604/415.000
IC [7]
ICM: A61M005-32
ICS: A61B019-00

L8 ANSWER 5 OF 10 USPATFULL
AN 2001:149472 USPATFULL
TI PROCESS AND DEVICE FOR INHALATION OF PARTICULATE MEDICAMENTS
IN VAN OORT, MICHIEL MARY, DURHAM, NC, United States
SACCHETTI, MARK JOSEPH, RALEIGH, NC, United States
PI US 2001018916 A1 20010906
AI US 1998-155388 A1 19980928 (9)
WO 1997-EP1560 19970325
None PCT 102(e) date
PRAI GB 1996-6677 19960329
DT Utility
FS APPLICATION
LN.CNT 775
INCL INCLM: 128/203.120
NCL NCLM: 128/203.120
IC [7]
ICM: A61M015-00
ICS: A61M016-10

L8 ANSWER 6 OF 10 USPATFULL

AN 2001:90260 USPATFULL
 TI Fatty acid-pharmaceutical agent conjugates
 IN Webb, Nigel L., Bryn Mawr, PA, United States
 Bradley, Matthews O., Laytonsville, MD, United States
 Swindell, Charles S., Merion, PA, United States
 Shashoua, Victor E., Brookline, MA, United States
 PI US 2001002404 A1 20010531
 AI US 2000-730450 A1 20001205 (9)
 RLI Continuation of Ser. No. US 1996-651428, filed on 22 May 1996,
 ABANDONED
 DT Utility
 FS APPLICATION
 LN.CNT 2511
 INCL INCLM: 514/560.000
 INCLS: 514/558.000
 NCL NCLM: 514/560.000
 NCLS: 514/558.000
 IC [7]
 ICM: A61K031-20
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8 ANSWER 7 OF 10 USPATFULL
 AN 2001:190709 USPATFULL
 TI Stabilized preparations for use in metered dose inhalers
 IN Weers, Jeffry G., San Diego, CA, United States
 Schutt, Ernest G., San Diego, CA, United States
 Dellamary, Luis A., San Marcos, CA, United States
 Tarara, Thomas E., San Diego, CA, United States
 Kabalnov, Alexey, Corvallis, OR, United States
 PA Inhale Therapeutic Systems, Inc., San Carlos, CA, United States (U.S.
 corporation)
 PI US 6309623 B1 20011030
 AI US 1998-218212 19981222 (9)
 RLI Continuation of Ser. No. WO 1998-US20615, filed on 29 Sep 1998
 Continuation-in-part of Ser. No. US 1998-133848, filed on 14 Aug 1998,
 now abandoned Continuation-in-part of Ser. No. US 1998-106932, filed on
 29 Jun 1998, now abandoned
 PRAI US 1997-60337 19970929 (60)
 DT Utility
 FS GRANTED
 LN.CNT 2644
 INCL INCLM: 424/045.000
 INCLS: 424/046.000; 424/489.000
 NCL NCLM: 424/045.000
 NCLS: 424/046.000; 424/489.000
 IC [7]
 ICM: A61K009-12
 EXF 424/45; 424/46; 424/489
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8 ANSWER 8 OF 10 USPATFULL
 AN 2001:86043 USPATFULL
 TI Medicament carrier with agglomerated large medicament particles and
 related method of manufacture thereof
 IN Van Oort, Michiel Mary, Durham, NC, United States
 Sacchetti, Mark Joseph, Raleigh, NC, United States
 PA Glaxo Wellcome Inc., Research Triangle Park, NC, United States (U.S.
 corporation)
 PI US 6245339 B1 20010612
 WO 9804308 19980205

AI US 1999-230613 19990128 (9)
 WO 1997-EP4128 19970730
 19990128 PCT 371 date
 19990128 PCT 102(e) date
 PRAI GB 1996-16047 19960731
 DT Utility
 FS GRANTED
 LN.CNT 938
 INCL INCLM: 424/400.000
 INCLS: 128/203.120; 128/203.130; 128/203.150; 128/203.190; 128/203.210;
 128/203.230
 NCL NCLM: 424/400.000
 NCLS: 128/203.120; 128/203.130; 128/203.150; 128/203.190; 128/203.210;
 128/203.230
 IC [7]
 ICM: A61K009-00
 ICS: A61M015-00; A61M016-10; A61M016-00
 EXF 424/400; 128/203.12; 128/203.13; 128/203.15; 128/203.19; 128/203.21;
 128/203.23

 L8 ANSWER 9 OF 10 USPATFULL
 AN 2000:76042 USPATFULL
 TI Metering apparatus
 IN Dwivedi, Sarvajna Kumar, San Diego, CA, United States
 Roberts, II, William Leroy, Apex, NC, United States
 Sacchetti, Mark Joseph, Raleigh, NC, United States
 Van Oort, Michiel Mary, Durham, NC, United States
 PA Glaxo Wellcome Inc., Research Triangle Park, NC, United States (U.S.
 corporation)
 PI US 6076522 20000620
 WO 9744080 19971127
 AI US 1998-180648 19981112 (9)
 WO 1997-EP2594 19970522
 19981112 PCT 371 date
 19981112 PCT 102(e) date
 PRAI GB 1996-10821 19960523
 DT Utility
 FS Granted
 LN.CNT 1090
 INCL INCLM: 128/203.150
 INCLS: 128/203.120
 NCL NCLM: 128/203.150
 NCLS: 128/203.120
 IC [7]
 ICM: A61M015-00
 EXF 128/203.15; 128/203.12; 128/203.21

 L8 ANSWER 10 OF 10 USPATFULL
 AN 1998:98932 USPATFULL
 TI DHA-pharmaceutical agent conjugates of taxanes
 IN Shashoua, Victor E., Brookline, MA, United States
 Swindell, Charles S., Merion, PA, United States
 Webb, Nigel L., Bryn Mawr, PA, United States
 Bradley, Matthews O., Laytonsville, MD, United States
 PA Neuromedica, Inc., Conshohocken, PA, United States (U.S. corporation)
 PI US 5795909 19980818
 AI US 1996-651312 19960522 (8)
 DT Utility
 FS Granted
 LN.CNT 2451

INCL INCLM: 514/449.000
INCLS: 514/549.000
NCL NCLM: 514/449.000
NCLS: 514/549.000
IC [6]
ICM: A61K031-335
ICS: A61K031-22
EXF 514/449; 514/549
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d 2 ab bib kwic

L8 ANSWER 2 OF 10 USPATFULL

AB Stabilized dispersions are provided for the delivery of a bioactive agent to the respiratory tract of a patient. The dispersions preferably comprise a plurality of perforated microstructures dispersed in a suspension medium that typically comprises a hydrofluoroalkane propellant. As density variations between the suspended particles and suspension medium are minimized and attractive forces between microstructures are attenuated, the disclosed dispersions are particularly resistant to degradation, such as, by settling or flocculation. In particularly preferred embodiments, the stabilized dispersions may be administered to the lung of a patient using a

metered

dose inhaler.

AN 2001:217988 USPATFULL

TI Stabilized preparations for use in metered dose inhalers

IN Weers, Jeffry G., San Diego, CA, United States
Schutt, Ernest G., San Diego, CA, United States
Dellamary, Luis A., San Marcos, CA, United States
Tarara, Thomas E., San Diego, CA, United States
Kabalnov, Alexey, Corvallis, OR, United States

PI US 2001046474 A1 20011129

AI US 2001-862764 A1 20010521 (9)

RLI Division of Ser. No. US 1998-218212, filed on 22 Dec 1998, PENDING
Continuation of Ser. No. WO 1998-US20615, filed on 29 Sep 1998, UNKNOWN
Continuation-in-part of Ser. No. US 1998-133848, filed on 14 Aug 1998,
ABANDONED Continuation-in-part of Ser. No. US 1998-106932, filed on 29
Jun 1998, ABANDONED

PRAI US 1997-60337 19970929 (60)

DT Utility

FS APPLICATION

LREP INHALE THERAPEUTIC SYSTEMS, INC, 150 INDUSTRIAL ROAD, SAN CARLOS, CA,
94070

CLMN Number of Claims: 150

ECL Exemplary Claim: 1

DRWN 4 Drawing Page(s)

LN.CNT 2850

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . 1.287

CFC-114	1.288
PFOB	1.305
Mannitol	1.333
Ethanol	1.361
n-octane	1.397
DMPC	1.43
Pluronic F-68	1.43
Sucrose	1.538
Hydroxyethylstarch	1.54

Sodium chloride 1.544

DETD . . . amino acids are further held to be within the scope of the present invention. The inclusion of both inorganic (e.g. **sodium chloride**, calcium chloride), organic salts (e.g. sodium citrate, sodium ascorbate, magnesium gluconate, sodium gluconate, tromethamine hydrochloride) and buffers is also contemplated.

DETD . . . inhibitors, e.g. cromolyn sodium; antiinfectives, e.g. cephalosporins, macrolides, quinolones, penicillins, streptomycin, sulphonamides, tetracyclines and pentamidine; antihistamines, e.g. methapyrilene; anti-inflammatories, e.g. **fluticasone propionate**, beclomethasone dipropionate, flunisolide, budesonide, tripedane, cortisone, prednisone, prednisilone, dexamethasone, betamethasone, or triamcinolone acetonide; antitussives, e.g. noscapine; bronchodilators, e.g. ephedrine, adrenaline, fenoterol, **formoterol**, isoprenaline, metaproterenol, salbutamol, albuterol, salmeterol, terbutaline; diuretics, e.g. amiloride; anticholinergics, e.g. ipatropium, atropine, or oxitropium; lung surfactants e.g. Surfaxin, Exosurf, . . .

DETD . . . and osmotic agents (to provide isotonicity, hyperosmolarity, or hyposmolarity). Examples of suitable salts include sodium phosphate (both monobasic and dibasic), **sodium chloride**, calcium phosphate, calcium chloride and other physiologically acceptable salts.

DETD [0173] 3.25% w/v **Sodium chloride** (Mallinckrodt, St. Louis, Mo.)

CLM What is claimed is:

. . . 29. The stable respiratory dispersion of claim 1 wherein said bioactive agents are selected from the group consisting of budesonide, **fluticasone propionate**, salmeterol, **formoterol** and DNase.

. . . 150. The stable respiratory dispersion of claim 133 wherein said bioactive agents are selected from the group consisting of budesonide, **fluticasone propionate**, salmeterol, **formoterol** and DNase.

=> d 7 ab bib kwic

L8 ANSWER 7 OF 10 USPATFULL

AB Stabilized dispersions are provided for the delivery of a bioactive agent to the respiratory tract of a patient. The dispersions preferably comprise a plurality of perforated microstructures dispersed in a suspension medium that typically comprises a hydrofluoroalkane propellant. As density variations between the suspended particles and suspension medium are minimized and attractive forces between microstructures are attenuated, the disclosed dispersions are particularly resistant to degradation, such as, by settling or flocculation. In particularly preferred embodiments, the stabilized dispersions may be administered to the lung of a patient using a metered dose inhaler.

AN 2001:190709 USPATFULL

TI Stabilized preparations for use in metered dose inhalers

IN Weers, Jeffrey G., San Diego, CA, United States
Schutt, Ernest G., San Diego, CA, United States
Dellamary, Luis A., San Marcos, CA, United States

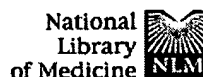
Tarara, Thomas E., San Diego, CA, United States
Kabalinov, Alexey, Corvallis, OR, United States
PA Inhale Therapeutic Systems, Inc., San Carlos, CA, United States (U.S. corporation)
PI US 6309623 B1 20011030
AI US 1998-218212 19981222 (9)
RLI Continuation of Ser. No. WO 1998-US20615, filed on 29 Sep 1998
Continuation-in-part of Ser. No. US 1998-133848, filed on 14 Aug 1998, now abandoned
Continuation-in-part of Ser. No. US 1998-106932, filed on 29 Jun 1998, now abandoned
PRAI US 1997-60337 19970929 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Bawa, Raj
LREP Rafa, Michael J., Cagan, Felissa H.
CLMN Number of Claims: 93
ECL Exemplary Claim: 1
DRWN 17 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 2644
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . 1.287
CFC-114 1.288
PFOB 1.305
Mannitol 1.333
Ethanol 1.361
n-octane 1.397
DMPC 1.43
Pluronic F-68 1.43
Sucrose 1.538
Hydroxyethylstarch 1.54
Sodium chloride 1.544
DETD . . . amino acids are further held to be within the scope of the present invention. The inclusion of both inorganic (e.g. **sodium chloride**, calcium chloride), organic salts (e.g. sodium citrate, sodium ascorbate, magnesium gluconate, sodium gluconate, tromethamine hydrochloride) and buffers is also contemplated.
DETD . . . inhibitors, e.g. cromolyn sodium; antiinfectives, e.g. cephalosporins, macrolides, quinolones, penicillins, streptomycin, sulphonamides, tetracyclines and pentamidine; antihistamines, e.g. methapyrilene; anti-inflammatories, e.g. **fluticasone propionate**, beclomethasone dipropionate, flunisolide, budesonide, tripedane, cortisone, prednisone, prednisilone, dexamethasone, betamethasone, or triamcinolone acetonide; antitussives, e.g. noscapine; bronchodilators, e.g. ephedrine, adrenaline, fenoterol, **formoterol**, isoprenaline, metaproterenol, salbutamol, albuterol, salmeterol, terbutaline; diuretics, e.g. amiloride; anticholinergics, e.g. ipatropium, atropine, or oxitropium; lung surfactants e.g. Surfaxin, Exosurf, . . .
DETD . . . and osmotic agents (to provide isotonicity, hyperosmolarity, or hyposmolarity). Examples of suitable salts include sodium phosphate (both monobasic and dibasic), **sodium chloride**, calcium phosphate, calcium chloride and other physiologically acceptable salts.
DETD Solution 1
3.9% w/v m-HES hydroxyethylstarch (Ajinomoto, Tokyo, Japan)
3.25% w/v **Sodium chloride** (Mallinckrodt, St. Louis, MO)
2.83% w/v Sodium phosphate, dibasic (Mallinckrodt, St. Louis, MO)
0.42% w/v Sodium phosphate, monobasic (Mallinckrodt, St. Louis, MO)

Solution. . .

CLM What is claimed is:

- . . . 29. The stable respiratory dispersion of claim 1 wherein said bioactive agents are selected from the group consisting of budesonide, **fluticasone propionate**, salmeterol, **formoterol**, gentamicin, LHRH, and DNase.
- . . . 87. The stable respiratory dispersion of claim 72 wherein said bioactive agents are selected from the group consisting of budesonide, **fluticasone propionate**, salmeterol, **formoterol** and DNase.

=>



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Inhaled salmeterol/fluticasone propionate combination. A pharmacoeconomic review of its use in the management of asthma.

Markham A, Adkins JC.

Adis International Limited, Auckland, New Zealand.

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Cost estimates from developed countries indicate that asthma accounts for up to 2% of the economic cost of all diseases. A large proportion of asthma-related costs are attributable to poor asthma control. Treatment strategies which improve clinical outcomes in patients with asthma, therefore, have the potential for significant economic benefits, and it is important to evaluate new asthma therapies for cost effectiveness. Several studies have established that salmeterol and fluticasone propionate combined in a single dry powder inhalation device are at least as effective as a combination of the 2 drugs administered via separate dry powder inhalers and more effective than monotherapy with fluticasone propionate or budesonide. Importantly, pharmacoeconomic analysis of several of these studies show that the salmeterol/fluticasone propionate combination is cost effective relative to monotherapy with fluticasone propionate or budesonide. Although the total cost of asthma management tended to be slightly higher with salmeterol/fluticasone propionate than with inhaled corticosteroid monotherapy; in most cases mean cost-effectiveness ratios were lower (i.e. more favourable) for salmeterol/fluticasone propionate than either fluticasone propionate or budesonide. Cost effectiveness was assessed according to 3 end-points: successfully treated weeks, symptom-free days and episode-free days. Mean cost-effectiveness ratios consistently favoured salmeterol/fluticasone propionate over the comparator drug for the end-point successfully treated weeks, and in most cases the other 2 end-points also favoured the combination product over the comparator. In a further study, salmeterol/fluticasone was also less costly than therapy with formoterol and budesonide administered via 2 separate inhalers. Studies of health-related quality of life (HR-QOL) using the Asthma Quality of Life Questionnaire indicate that salmeterol/fluticasone propionate produces clinically meaningful improvements in overall HR-QOL relative to salmeterol monotherapy or placebo. Improvements in overall HR-QOL were statistically significantly greater for salmeterol/fluticasone propionate than with fluticasone propionate or budesonide alone, although the differences between treatments did

not exceed the threshold for clinical significance. In conclusion, short term cost-effectiveness data show that salmeterol/fluticasone propionate is more cost effective than the inhaled corticosteroids budesonide and fluticasone propionate alone. The combination product also appears to improve HR-QOL relative to placebo or salmeterol alone.

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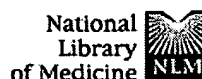
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Dose-response relationships in determining the safety:efficacy ratio.

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The development of inhaled agonists selective for beta 2-adrenoceptors and high potency corticosteroids has improved the treatment of asthma. The delivery of the drugs to the site of action reduces the systemic exposure and hence reduces adverse systemic events. Together, these factors have resulted in improved toxicity: therapeutic ratios. Long-acting beta 2-agonists, such as salmeterol and formoterol, and high efficacy corticosteroids, such as fluticasone propionate and budesonide, now are available for clinical use. Because suboptimal treatment of asthma causes increased morbidity and mortality, and increased costs to society, these compounds are of particular value. Risk factors associated with fatal and near-fatal asthma have been identified, and it would appear that drug treatment by metered dose inhaler per se does not cause increased asthma fatality as an independent risk factor.

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